NUCLEOTIDES®
Saúde intestinal e restauração imunológica, inclusive em crianças
http://aformulabr.com.br/qrcode/nucleotidesafv01.pdf
NUCLEOTIDES®

Saúde intestinal e restauração imunológica, inclusive em crianças

DESCRIÇÃO

Nucleotides® é um concentrado produzido a partir da fermentação de Saccharomyces cerevisiae e padronizado em 60% de nucleotídeos, isento de alergênicos e GMO.

MECANISMO DE AÇÃO

Nucleotides® atua na ampliação da resposta imune e na manutenção da saúde intestinal, isso porque a renovação celular desses sistemas é mais acelerada, necessitando uma quantidade maior de nucleotídeos para seu funcionamento, principalmente com estresse, infecções ou exercício físico intenso. No sistema imune, Nucleotides® induz a resposta imune celular via Th1, elevando a interleucina-12 (IL-12), o que ocasiona o aumento da resistência contra patógenos e melhora a capacidade fagocítica dos macrófagos. Nucleotides® atua também reduzindo a concentração de IgE, principal imunoglobulina presente na reação alérgica, aumentando a concentração de IgM (importante nas infecções de fase aguda) e IgA (responsável pela proteção da mucosa). Nucleotides® promove ainda aumento na produção de IgG contra antígenos de Haemophilus Influenzae tipo B após a terceira imunização em crianças. Já no intestino, Nucleotides® auxilia na manutenção da barreira íntegra, impedindo a entrada de patógenos no organismo e mantendo a microbiota intestinal, funcionando como um prebiótico.

INDICAÇÕES

✓ Imunidade (inclusive gripes e resfriados)
✓ Estresse elevado;
✓ Saúde intestinal;
✓ Exercícios físicos intensos.

DOSE USUAL

Recomendação oral de 300 a 500mg de Nucleotides® ao dia; sublingual de 50mg de Nucleotides® ao dia.

SUGESTÕES DE FÓRMULAS

<table>
<thead>
<tr>
<th>Nucleotides®</th>
<th>500mg</th>
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<tbody>
<tr>
<td>Dimpless®</td>
<td>10mg</td>
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<tr>
<td>Vitamina C</td>
<td>100mg</td>
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<tr>
<td>Vitamina E</td>
<td>80mg</td>
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<tr>
<td>Coenzima Q10</td>
<td>20mg</td>
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</tbody>
</table>

Modo de uso: 1 dose, 1 vez ao dia.
Indicação: reforço da imunidade e ação antioxidante.

<table>
<thead>
<tr>
<th>Nucleotides®</th>
<th>50mg/dose</th>
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<tr>
<td>Gotas sublinguais qsp.</td>
<td>1 dose</td>
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Modo de uso: 1 dose ao dia.
Indicação: manutenção da saúde intestinal em crianças.

PRINCIPAIS REFERÊNCIAS


The role of nucleotides in the immune and gastrointestinal systems: potential clinical applications.

Nucleotides are low molecular weight biological molecules key to biochemical processes. Sources include de novo synthesis, recovery via salvage mechanisms, and dietary intakes. Although endogenous production serves as the main nucleotide source, evidence suggests that exogenous sources are essential to immune competence, intestinal development, and recovery. Dietary nucleotides serve a marked role in rapidly proliferating cells where they are necessary for optimal function. Accordingly, dietary nucleotides are deemed conditionally essential in the presence of various physiological stresses, including growth and development, recovery from injury, infection, and certain disease states. Clinical studies that evaluated nutrition formulations of nucleotides in combination with other specific nutrient substances demonstrated improved clinical outcomes in patients characterized as critically ill, injured, immune suppressed, or with chronic gastrointestinal conditions. However, conclusions regarding specific benefits of nucleotides are limited. Scientific substantiation of nucleotide supplementation in infant formula has been reported to improve the maturation and development of the intestinal tract as well as immune function. All medical nutrition products except for one immune-modulating formulation are devoid of nucleotides. In an effort to build on this, the current review presents the data to support potential clinical applications for nucleotides in enteral nutrition that may contribute to improved outcomes in physiologically stressed patients.

The role of nucleotides in human nutrition.

Dietary NT are reported to have significant effects upon lymphoid, intestinal and hepatic tissues, and lipid metabolism (Table 3). The mechanism remains unknown, and the nutritional role of NT remains controversial. However, maintenance of the endogenous NT supply via de novo synthesis and salvage is metabolically costly. Preformed NT supplied by the diet may contribute to tissue NT pools and thus optimize the metabolic function of rapidly dividing tissues such as those of the gastrointestinal and immune systems. An exogenous source of NT may be particularly important for individuals whose dietary intake of NT is low and/or whose tissue needs are increased, for example, rapidly growing infants fed most cow's milk-based formulas and individuals with disease related immunosuppression, intestinal, or liver injury. Under these conditions, dietary NTs may play a role as conditionally essential nutrients. In addition to serving as nucleic acid precursors, NTs and their related metabolic products are potent inter- and intracellular biological mediators. Certain effects of dietary NT may relate to one or more of these important functions.

Dietary nucleotides: effects on the immune and gastrointestinal systems.

Nucleotides (NT) and their related metabolic products play key roles in many biological processes. NT can be synthesized endogenously and thus are not considered essential nutrients. Studies have demonstrated, however, that dietary NT can have beneficial effects; the term “conditionally essential” has been used to describe their role in human nutrition. These nutrients may become essential when the endogenous supply is insufficient for normal function, even though their absence from the diet does not lead to a classic clinical deficiency syndrome. Most dietary NT are rapidly metabolized and excreted. However, some are incorporated into tissues, particularly at younger ages and with fasting. Under conditions of limited NT intake, rapid growth or certain disease states, dietary NT may spare the cost of de novo NT synthesis and optimize the function of rapidly dividing tissues such as those of the gastrointestinal and immune systems. Animals fed NT-supplemented versus non-NT supplemented diets have enhanced gastrointestinal growth and maturation, and improved recovery following small and large bowel injury. Indices of humoral and cellular immunity are enhanced, and survival rates are higher following infection with pathogens. Infants receive NT in human milk, where they are present as nucleic acids, nucleosides, nucleotides and related metabolic products. The NT content of human milk is significantly higher than most cow's milk-based infant formulae. Dietary NT are reported to enhance the gastrointestinal and immune systems of formula-fed infants. Infants fed NT-supplemented versus non-supplemented formula have a lower incidence of diarrhea, higher antibody titers following Haemophilus influenzae type b vaccination and higher natural killer cell activity. These data suggest that human milk NT may contribute to the superior clinical performance of the breastfed infant.
Modulation of the immune response mediated by dietary nucleotides.

Dietary nucleotides have been reportedly beneficial, especially for infants, since they positively influence lipid metabolism, immunity, and tissue growth, development and repair. Rapidly proliferating tissues, such as the immune system or the intestine are not able to fulfil the needs of cell nucleotides exclusively by de novo synthesis and they preferentially utilize the salvage pathway recovering nucleosides and nucleobases from blood and diet. In the present review we describe the modulatory effect of dietary nucleotides on the immune system together with some of their effects on gut-associated lymphoid tissue. Dietary nucleotides influence lymphocyte maturation, activation and proliferation. Likewise, they affect the lymphocyte subset populations in both the small intestine and blood. Moreover, they are involved in enhancing macrophage phagocytosis and delayed hypersensitivity as well as allograft and tumour responses. In addition, they contribute to the immunoglobulin response in early life, having a positive effect on infection. In fact the incidence and duration of acute diarrhoea is lower in infants fed supplemented-nucleotide formulas. The molecular mechanisms by which dietary nucleotides modulate the immune system are practically unknown. Dietary nucleotides have been shown to enhance the production and the genetic expression of IL-6 and IL-8 by foetal small intestinal explants. Dietary nucleotides may influence protein biosynthesis as well as signal membrane transduction mediated by the interaction of exogenous nucleosides and their receptors may also contribute to modulate the expression of a number of genes, some of which can directly affect the levels of intestinal cytokines.

Dietary nucleotides can up-regulate antigen-specific Th1 immune responses and suppress antigen-specific IgE responses in mice.

BACKGROUND: It has been reported that dietary nucleotides enhance T helper cell activities. In this study, we have determined the effects of dietary nucleotides on antigen-specific Th1 and Th2 responses and IgE responses. METHODS: Ovalbumin (OVA)-specific T cell receptor (TCR) transgenic (OVA-TCR Tg) mice, 3 weeks old, were fed a nucleotide-free diet (NT(-) diet) or the NT(-) diet supplemented with dietary nucleotides (NT(+)) for 4 weeks. Cytokine production by spleen cells and macrophages obtained from these mice was measured in vitro. BALB/c mice, 3 weeks old, immunized intraperitoneally with OVA adsorbed onto alum, were fed the NT(-) diet or the NT(+) diet for 4 weeks. Serum levels of antigen-specific antibodies in the BALB/c mice were determined by ELISA. RESULTS: The level of production of antigen-specific interferon-gamma by spleen cells was significantly higher in the OVA-TCR Tg mice fed the NT(+) diet than in the control mice. The levels of secretion of bioactive IL-12 by spleen cells and peritoneal macrophages were also significantly increased in the NT(+)-diet group. The serum OVA-specific IgE level was significantly decreased in BALB/c mice fed the NT(+) diet compared with those fed the NT(-) diet. CONCLUSION: These results show that dietary nucleotides up-regulate the antigen-specific Th1 immune response through the enhancement of IL-12 production and suppress the antigen-specific IgE response.

Modulation of the immune system by human milk and infant formula containing nucleotides.

OBJECTIVE: To determine whether human milk and nucleotides added to infant formula at levels present in human milk enhance development of the immune system during infancy. METHODS: A 12-month, controlled, randomized and blinded, multisite feeding trial was conducted on two infant formulas: iron-fortified, milk-based control formula (Control) or the same formula fortified with nucleotides (Nucleotide). The level (72 mg/L) and ratio of individual nucleotides selected were patterned after those available in human milk. A third group fed human milk exclusively for 2 months and then human milk or Similac with iron until 12 months of age also was studied. Response to immunizations was chosen to assess development of the immune system. Infants followed the immunization schedule recommended by the American Academy of Pediatrics in 1991. OUTCOME VARIABLES: Antibody responses were determined at 6, 7, and 12 months of age to Haemophilus influenzae type b polysaccharide (Hib), to diphtheria and tetanus toxoids, and to oral polio virus (OPV) immunizations. RESULTS: Of 370 full-term, healthy infants enrolled, 311 completed the study (107
Control, 101 Nucleotide, 103 human milk/Similac with iron). Intake, tolerance, and growth of infants were similar in all three groups. Compared with the Control group 1 month after the third immunization (7 months of age), the Nucleotide group had a significantly higher Hib antibody concentration (geometric mean concentrations of 7.24 vs 4.05 micrograms/mL, respectively), and a significantly higher diphtheria antibody concentration (geometric mean of 1.77 vs 1.38 U/mL). The significantly higher Hib antibody response in the Nucleotide group persisted at 12 months. The antibody responses to tetanus and OPV were not enhanced by nucleotide fortification. There also was an effect of breastfeeding on immune response. Infants who breastfed had significantly higher neutralizing antibody titers to polio virus than either formula-fed group (1:346 vs 1:169 and 1:192 in the Control and Nucleotide groups, respectively) at 6 months of age. CONCLUSION: Infant formula fortified with nucleotides enhanced H influenzae type b and diphtheria humoral antibody responses. Feeding human milk enhanced antibody responses to OPV. Dietary factors play a role in the antibody response of infants to immunization.

Dietary nucleotide improves markers of immune response to strenuous exercise under a cold environment.

BACKGROUND: Strenuous exercise has been classically associated to immune-suppression and consequently to an increased risk of infections, especially at the upper respiratory tract. The administration of dietary nucleotides has been demonstrated useful to maintain the immune function in situations of stress and thus could be an appropriate strategy to counteract the decline of the immune function associated to strenuous exercise. The aim of the present study was to assess the impact of a specific nucleotide formulation (Inmunactive®) on the markers of immune function of athletes after a heavy exercise bout under cold conditions. METHODS: Twenty elite male taekwondo athletes were randomly divided into two groups of 10 subjects that were supplemented with placebo (P) or Inmunactive (I) at 480 mg/day during 30 days. At baseline (day 0) and after 4 wk of supplementation (day 30) each subject undertook an exhaustion exercise test using a cycloergometer. Skin temperature, core temperature, heart rate, lactate concentration and rating of perceived exertion (RPE) were recorded during the test. Blood and saliva samples were obtained before and after each exercise test for determination of blood cell concentrations, PHA-stimulated lymphocyte proliferation (PHA-LP) and salivary immunoglobulin A (SIgA). RESULTS: Exercise tests induced neutrophilia and reduction in lymphocyte blood counts on day 0 and on day 30 in both groups. However, the I group exhibited a faster recovery from the lymphopenic response than the P group, so that lymphocyte levels were higher after 150 min (P < 0.0028). Furthermore, the lymphoproliferative response was modulated by nucleotide supplementation, since it was higher in the I group on day 30 despite an almost significant (P < 0.06) exercise-evoked decrease at baseline. CONCLUSIONS: These findings suggest that supplementation with a nucleotide-based product for 4 weeks could counteract the impairment of immune function after heavy exercise.

Effects of Dietary Nucleotides on Immune Responses.

In this study, the effects of dietary nucleotides on the immune response balance between T helper cells type 1 (Th1) and type 2, and on the mucosal immune response in weanling mice were investigated. It was demonstrated that dietary nucleotides up-regulate the Th1 immune response and suppress the antigen-specific IgE antibody response in weanling mice. Thus, the results suggest that dietary nucleotides may be beneficial for the prevention of allergic diseases in early infancy. In addition, it was shown that dietary nucleotides increased the proportion of a γδT-cell receptor (TCR) - bearing intestinal intraepithelial lymphocyte (IEL) subset, IL-7 production by intestinal epithelial cells and the antigen-specific IgA response. Therefore, the present study indicates that dietary nucleotides may have an effect on the mucosal intranet in the intestinal mucosal immune system.
Dietary nucleotides and early growth in formula-fed infants: a randomized controlled trial.

BACKGROUND: Dietary nucleotides are nonprotein nitrogenous compounds that are found in high concentrations in breast milk and are thought to be conditionally essential nutrients in infancy. A high nucleotide intake has been suggested to explain some of the benefits of breastfeeding compared with formula feeding and to promote infant growth. However, relatively few large-scale randomized trials have tested this hypothesis in healthy infants. OBJECTIVE: We tested the hypothesis that nucleotide supplementation of formula benefits early infant growth. PATIENTS AND METHODS: Occipitofrontal head circumference, weight, and length were assessed in infants who were randomly assigned to groups fed nucleotide-supplemented (31 mg/L; n=100) or control formula without nucleotide supplementation (n=100) from birth to the age of 20 weeks, and in infants who were breastfed (reference group; n=101). RESULTS: Infants fed with nucleotide-supplemented formula had greater occipitofrontal head circumference at ages 8, 16, and 20 weeks than infants fed control formula (mean difference in z scores at 8 weeks: 0.4 [95% confidence interval: 0.1-0.7]; P=.006) even after adjustment for potential confounding factors (P=.002). Weight at 8 weeks and the increase in both occipitofrontal head circumference and weight from birth to 8 weeks were also greater in infants fed nucleotide-supplemented formula than in those fed control formula. CONCLUSIONS: Our data support the hypothesis that nucleotide supplementation leads to increased weight gain and head growth in formula-fed infants. Therefore, nucleotides could be conditionally essential for optimal infant growth in some formula-fed populations. Additional research is needed to test the hypothesis that the benefits of nucleotide supplementation for early head growth, a critical period for brain growth, have advantages for long-term cognitive development.

Sublingual Nucleotides Prolong Run Time to Exhaustion in Young Physically Active Men.

Abstract: Although dietary nucleotides have been determined to be required for normal immune function, there is limited direct interventional evidence confirming performance-enhancing effects of sublingual nucleotides in humans. A double-blind, placebo-controlled, randomized trial was conducted to evaluate the effect of sublingual nucleotides (50 mg/day) administered for 14 days in thirty young healthy physically active males, on endurance performance and immune responses. Fasting white blood cell count, natural killer cells (NKC) number, NKC cytotoxic activity, and serum immunoglobulin (IgA, IgM, IgG), and time to exhaustion, peak rate of perceived exertion, peak heart rate, and peak running speed during the exercise test were measured at baseline (day 0) and post-intervention (day 14). Time to exhaustion, as well as serum immunoglobulin A and NKC cytotoxic activity, were significantly higher at day 14 (p < 0.05) in participants supplemented with nucleotides compared with those who consumed placebo. No significant differences in other parameters were observed between groups at post-intervention. No volunteers withdrew before the end of the study nor reported any vexatious side effects of supplementation. The results of the present study suggest that sublingual nucleotides may provide pertinent benefit as both an ergogenic and immunostimulatory additive in active males.
REFERÊNCIAS


